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09/937,137	09/21/2001	Giammaria Sitar	1271-001	4515

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EXAMINER

AFREMOVA, VERA

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/937,137

Applicant(s)

SITAR, GIAMMARIA

Examiner

Vera Afremova

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-6,8-12,14-21 and 25-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,8-12,14-21 and 25-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/24/2005</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/24/2005 has been entered.

Claims 1, 3-6, 8-12, 14-21 as amended and new claims 25-28 are pending and under examination.

Claims 2, 7, 13 and 22-24 were canceled by applicant.

### ***Claim Rejections - 35 USC § 112***

#### ***Indefinite***

Claims 1, 3-6, 8-12, 14-21 as amended and new claims 25-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the claimed method is intended for making a preparation of fetal nucleated red blood cells (fetal NRBCs) but it does lead to a preparation of fetal NRBCs because final step is ascertaining the presence of fetal NRBCs in a mixed cell fraction. In alternative, it is unclear what is a preparation of fetal nucleated red blood cells as intended for a final goal.

Claims 11 and 25 are rendered indefinite by the phrase “substantial” separation in the lack of definitions. It is unclear as claimed what amount or percent is encompassed by the claimed phrase “substantial” separation. The specification describes that “most” of NRBCs are found in interface with separating medium and “most” of lymphocytes and monocytes sink down (page 6, lines 1-4), the specification also describes that the low density fraction floating at interface contains “most” NRBCs together with “some” lymphocytes and monocytes (page 110, lines 16-19). However, the percent or the amount is intended for “most” or “some” cells is not described. Thus, the claimed term “substantial” separation is uncertain in the light of specification.

Claims 20, 21, and 28 remain/are indefinite with respect to the claimed phrase “a single separation step”. The claimed method encompasses at least two steps including step of forming a non-physiological mixture of a blood sample and step of centrifugation. Thus, the claimed method does not appear to be one (single) step separation method. In alternative, the method comprises identification of NRBCs in the whole low density fraction of nucleated cells comprising NRBCs together with at least some lymphocytes and monocytes. Thus, the scope of claims does not appear to encompass a “single separation step” of nucleated cells because the claimed method includes at least two steps such as step of removal of one mixed cellular fraction and step of identification of various cells in one removed mixed cellular fraction.

***New matter***

Claims 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not

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described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Insertion of the limitation "13000 nucleated cells" in claims 26 and 27 has no support in the as-filed specification. The insertion of this limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus that would show possession of the concept of the use of "13000 nucleated cells".

There is only (one) exemplified disclosure (table 3) that contains information about numbers of cells from maternal blood samples wherein the presently claimed number is not present as written.

This is not sufficient support for the new genus as claimed. This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of the limitation "13000 nucleated cells" in claims 26 and 27 is considered to be the insertion of new matter for the above reasons.

### ***Scope of enablement***

Claims 11, 12, 14-21 as amended and new claims 25-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ascertaining the presence of fetal NRBCs in the whole low density fraction of nucleated cells comprising

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NRBCs, lymphocytes and monocytes, does not reasonably provide enablement for physical or “substantial” separation of NRBCs from lymphocytes and monocytes in blood. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Nature of the invention relates to detection of fetal cells circulating in maternal blood as intended for prenatal diagnosis (specification page 1).

Breadth of the claims is drawn to physical or to “substantial” physical separation of NRBCs from lymphocytes and monocytes in a mixture comprising maternal blood sample.

Amount of guidance and working examples are limited to removal of a low density cellular fraction (density  $<1.068$  g/ml) floating at the interface between plasma and medium after centrifugation. The low density cellular fraction is said to contains “most” NRBCs present in starting blood together with “some” lymphocytes and monocytes as disclosed (page 10, lines 13-20). Thus, there is no protocol of “substantial” physical separation of NRBCs from lymphocytes and monocytes. No quantitative analysis for physical separation of NRBCs from lymphocytes and monocytes is disclosed. The final product contains more or less NRBCs together with more or less lymphocytes and monocytes.

The prior art (IDS reference; Sitar et al. Hematologica. 1997, 82; 5-10) and the applicant's admission demonstrates that densities of NRBCs, lymphocytes and monocytes are overlapping (page 3) including density  $<1.068$  g/ml that are used in the instant method (page 10). Thus, the state of the prior art demonstrates unpredictability in physical separation of NRBCs from lymphocytes and monocytes due to their overlapping density ranges.

Furthermore, the specification describes that the starting mixture for cell separation is made by combining maternal blood with a culture medium and ACD (acid-citrate-dextrose, page 9) in order to form a “non-physiological” conditions as disclosed on page 9 or 5. The “non-physiological” conditions are believed to decrease the density of NRBCs and to increase the density of lymphocytes and monocytes (page 5, lines 10-15). However, this is not clearly shown by applicant. But the limitation drawn the use of generic “non-physiological” conditions including the use of a singled out low pH condition is encompassed by the claimed invention. However, no single condition from those that are described is clearly pointed as being critical for modifying cell density as believed (page 5). No quantitative analysis is disclosed for physical separation of NRBCs from lymphocytes and monocytes that would result from using “non-physiological” conditions or low pH as claimed. Moreover, no comparative showing with “physiological” conditions is disclosed.

Thus, the concept of physical or “substantial” separation of NRBCs from lymphocytes and monocytes by using generic “non-physiological” conditions or by using a singled-out low pH condition is not being enabled. Applicant demonstrates only the presence of fetal cells in the whole low density maternal blood cell fraction (table 3) but not a physical separation of NRBCs from lymphocytes and monocytes in maternal blood.

The prior art and applicant’s admission demonstrates that densities of NRBCs, lymphocytes and monocytes are overlapping (page 3). Thus, the state of the prior art demonstrates unpredictability in physical or “substantial” separation of NRBCs from lymphocytes and monocytes. The criticality of generic “non-physiological” conditions for cell

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separation as claimed is not supported by quantitative showing as disclosed. The criticality of a low pH as a single “non-physiological” condition is not shown applicant.

Therefore, neither specification nor the prior art can be said to support the enablement of the claims over their breath.

Undue experimentation would be required to practice the invention as claimed due to the amount of experimentation necessary because of the limited amount of guidance and limited number of working examples in the specification, the nature of the invention, the state of the prior art, breadth of the claims and the unpredictability of the art.

As set forth in *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA) 1970: [Section 112] requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of the enablement varies inversely with the degree of unpredictability of the factors involved. *Ex parte Humphreys*, 24 USPQ2d, 1260.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-5, 8, 10-12, 14-21 as amended and new claims 25-28 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,641,628 (Bianchi) taken with US 5,676,849 (Sammons et al.); US 5,432,054 (Saunders et al.) and Guyton (Textbook of Medical Physiology. 8<sup>th</sup> edition. 1991, pages 276-280, 330-31, 752) as explained in the prior office action and repeated herein.



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Claims are directed to a method for isolating or preparing fetal nucleated red blood cells (NRBCs) present in maternal peripheral blood for prenatal genetic investigation wherein the method comprises step of combining a maternal blood sample with a medium in order to form a "non-physiological" mixture having specific characteristics that are pH 6.4-6.6, osmolarity 300-330 mOsm,  $\text{Na}^+$  150-160 mmol/l,  $\text{K}^+$  4.5-5.5 mmol/l,  $\text{Cl}^-$  100-115 mmol/l,  $\text{Ca}^{++}$  1.00 -2.50 mmol/l, glucose 400-500 mg/dl, lactate 10-20 mg/dl; step of transferring the mixture to a cell separation device and adding a high density liquid containing a red blood cell aggregating agent, step of isolating NRBCs by subjecting the separation device to centrifugal force, step of washing and resuspending the isolated NRBCs and step of identifying and counting fetal NRBCs. Some claims are further drawn to the use of a liquid containing a red blood cells aggregating agent such as Ficoll containing preparation. Some claims are further drawn to the use of a liquid in separation device with 1.068 g/ml density. Some claims are further drawn to the use a cell separation device or apparatus in a method for isolating fetal cells present in maternal peripheral blood for prenatal genetic investigation.

The cited patent US 5,641,628 (Bianchi et al.) is relied in the instant office action for the disclosure of methods for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation (example 10) wherein the method encompasses isolation of fetal nucleated red blood cells by density gradient centrifugation of maternal blood which has been modified by addition of a medium or citrate dextrose solution (col. 22, line 42). The cited patent also teaches steps of transferring the mixture to a cell separation device, adding a high density liquid with Ficoll, step of isolating mononuclear cells including NRBCs by subjecting the separation device to centrifugal force, step of washing and resuspending the isolated cells and

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step of identifying fetal NRBCs with antibodies to precursors of hematopoietic cells and by PCR techniques with Y chromosome primers.

The cited patent US 5,641,628 is silent with regard to the final characteristics of the modified blood sample. However, the claimed amounts for  $\text{Cl}^-$ ,  $\text{Ca}^{++}$ , and lactate are the same as in normal blood sample as evidenced by Guyton (page 277). Thus, the blood sample of the cited patent US 5,641,628 provides for the same amounts for  $\text{Cl}^-$ ,  $\text{Ca}^{++}$ , and lactate in the resulting blood mixture as encompassed by the claimed invention. The reference by Guyton also demonstrates that osmolarity of normal blood is about 302 mOsm that is within the presently claimed ranges. Thus, the blood sample of the cited patent US 5,641,628 provides for the same osmolarity as encompassed by the claimed invention. Further, osmolarity in the method of the cited patent US 5,641,628 is reasonably expected to be increased after addition of the aqueous citrate-dextrose solution. The presently claimed amounts for  $\text{Na}^+$  and  $\text{K}^+$  are about the same or slightly higher than in normal blood according to the reference by Guyton. But the citrate aqueous solution of the cited patent US 5,641,628 is likely to provide for additional sodium and/or potassium. The cited patent US 5,641,628 also suggests that the blood sample is stored overnight with the culture medium RPMI (col. 13, line 42) and, thus, the blood sample is reasonably expected to contain about the same amounts of potassium and/or sodium as encompassed by the claimed invention. The cited patent US 5,641,628 is silent about pH value. But the cited patent US 5,676,849 demonstrates that the commonly used citrate-dextrose/glucose aqueous solution contain citric acid (col. 6, line 58 or col. 10, lines 39). Thus, the solution in the method of US 5,641,628 is reasonably expected to provide for pH low that neutral in the method for fetal cells preparation or identification.

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The cited patent US 5,641,628 teaches the separation of cells by liquid density gradient centrifugation but it is silent about the liquid density in the method for separation of fetal cells from maternal blood. However, the cited patent US 5,432,054 teaches the use of liquid density gradient centrifugation for separation of fetal cells from maternal blood wherein the liquid density gradient includes 1.065 g/ml (col. 12, table 2) or about 1.068 g/ml for centrifugation of modified maternal blood as encompassed by the presently claimed method.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to practice a method for isolating fetal cells present in maternal peripheral blood for prenatal genetic investigation wherein the method encompasses isolation of fetal nucleated red blood cells by density gradient centrifugation of maternal blood modified by addition of acid-citrate-dextrose (glucose) preparation as taught and suggested by the cited patents US 5,641,628 (Bianchi) and US 5,676,849 (Sammons et al.) with a reasonable expectation of success in isolating fetal nucleated red blood cells as demonstrated by the cited patents. The concept of isolating fetal cells from maternal blood of the cited patents US 5,641,628 (Bianchi), US 5,676,849 (Sammons et al.) and US 5,432,054 (Saunders et al.) is based on a density gradient centrifugation isolation of fetal nucleated red blood cells in low density cell fraction from modified maternal blood and it is similar to the concept of the presently claimed method which is also based on a density gradient centrifugation isolation of fetal nucleated red blood cells from modified maternal blood. The characteristics of the resulting modified blood sample that are claimed appear to be about the same as encompassed by the cited US 5,641,628 (Bianchi et al.) as evidenced by Guyton. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary. One of skill in the art

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would have been motivated to used acid-citrate-dextrose solution (ACD) for the expected benefits in blood cell separation because addition of ACD is a common practice in the methods for separation of fetal cells from maternal blood as adequately demonstrated by the cited US 5,641,628 (Bianchi) and US 5,676,849 (Sammons et al.). Thus, the claimed subject matter fails to patentably distinguish over the state art as represented by the cited references.

Therefore, the claims are properly rejected under 35 USC § 103.

Claims 1, 3-5, 8, 10-12, 14-21 as amended and new claims 25-28 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,641,628 taken with US 5,676,849; US 5,432,054 and Guyton as applied to claims 1, 3-5, 7 and 8 above, and further in view of US 4,424,132; GB 2-75376 and FR 77 08053 as explained in the prior office action and repeated herein.

Claims 1, 3-5, 8, 10-12, 14-21, 25-28 as explained above. Claims 6 and 9 are further drawn to the use of a cell separation device or apparatus with elongated chamber and channel(s) that are open to the chamber in a method for isolating fetal cells present in maternal peripheral blood for prenatal genetic investigation.

The cited patents US 5,641,628; US 5,676,849 and US 5,432,054 are relied upon as explained above for the disclosure of methods for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation wherein the methods encompass isolation of fetal nucleated red blood cells by density gradient centrifugation of modified maternal blood in various cell separation devices. The cited patents are silent about design of cell separation devices. However, the methods of the cited patents encompass the use of generic cell

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separation devices and they result in successful separation of fetal cells. Thus, there is a reasonable belief that the cell separation devices of the cited patents are suitable and appropriate in the methods for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation.

Additional references US 4,424,132; GB 2-75376 and FR 77 08053 are relied upon to demonstrate a large variety of cell separation devices available in the prior art and suitable for cell separation in the present invention directed to a method for isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation. The devices of the cited patents comprise an elongated chamber and channel(s) that are open to the chamber.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use a large variety of cell separation devices suitable for separating blood cells including isolating nucleated fetal cells from maternal peripheral blood intended for prenatal genetic investigation as demonstrated by the cited references. The cited references are in the same field of endeavor and seek to solve the same problems as the instant application and claims such as blood cell separation, and one of skill in the art is free to select devices available in the prior art. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary. Moreover, the devices disclosed by the cited patents US 4,424,132; GB 2-75376 and FR 77 08053 are admitted by applicant as suitable in the presently claimed invention (specification page 6, par. 3). Thus, whatever differences might exist between various cell separation devices of the prior art and the particular device of the present invention, the claimed subject matter fails to patentably distinguish over the

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state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

***Response to Arguments***

Applicant's arguments filed 5/24/2005 have been fully considered but they are not all found persuasive.

Claim rejection under 35 U.S.C. 102(b) as being anticipated by Boyer et al. {Blood. June 1976. Vol. 47, No. 6, pages 883-897} has been withdrawn in the light of applicant's argument that the reference by Boyer et al. discloses a method for enrichment/separation of fetal red blood cells or erythrocytes that by definition have no nucleus but the claimed invention drawn to separation of nucleated red blood cells including fetal NRBCs (response page 11).

Claim rejection under 35 U.S.C. 102(a) as being anticipated by Giammaria Sitar et al. {Cytometry, April 1, 1999. Vol. 35, No. 4, pages 337-345} has been withdrawn in the light of Declaration under 37CFR 1.132 by applicant Giammaria Sitar filed on 5/24/2005.

As related to claim rejection under 35 U.S.C. 103(a) applicant's arguments (response pages 11-12) are based on contents of second Declaration under 37 CFR 1. 132 by Sitar filed 5/24/2005. The contents of Declaration are mostly drawn to the idea that pH values in the cited methods are likely to be outside of presently claimed ranges. The main argument is directed to the idea that the presently claimed invention is patentably distinct from the cited prior art on the basis on the pH range in the mixture of blood sample and additional medium (see Declaration page 3) and that the prior art does not recognize pH value as the result effective variable.

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This argument is not found particularly convincing in the lack of evidence that pH is a critical “non-physiological” condition in the “non-physiological” mixture that would result in separation of cell as claimed and as disclosed. The as-filed specification does not provide evidence related to pH criticality and it does not describe or it does not demonstrate that low pH causes “substantial” separation of the NRBCs including fetal NRBCs from the lymphocytes and monocytes. Although it might be true that different amounts of ACD could be used in the prior art method for modifying blood samples, the use of at least some amounts of ACD (acid-citrate-dextrose solution) is reasonably expected to provide for somehow lower pH than physiologically normal. Moreover, the cited prior art methods have been successful in detecting presence of fetal NRBCs in the low density cell fractions that are removed by centrifugation of blood samples in separating media including Ficoll.

Applicant also argues that the prior art methods comprise complex cell separation protocols and/or several centrifugation steps that are not “a single separation step” as claimed. This argument is not found convincing since the meaning of this limitation is indefinite. Moreover, the phrase “a single separation step” appears to encompass the use of a single centrifugation device for cell separation (claims 10 and 16).

With regard to the cited prior art applicant argues that centrifugation step in the methods of the cited reference is an initial step that results in separation of a mononuclear cell fraction {comprising fetal nucleated red blood cells and maternal monocytes and lymphocytes} and that the prior art methods require some additional steps for physical, true or substantial separation of fetal cells from maternal monocytes and lymphocytes, for example: by FACS, by differential hemolysis or by DNA analysis (declaration page 4). Yet, the claimed method does not result in

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the production of a pure fraction of fetal cells that are fully separated/isolated from maternal cells as result of one and only centrifugation step. The claimed method comprises step of centrifugation and the other step of “ascertaining the presence of fetal NRBCs” and, thus, the claimed method comprises both initial and additional steps in contradiction to the argument(s). Therefore, the cited prior art, that demonstrates the presence of fetal cells in a low density mononuclear cell fraction obtained by centrifugation, teaches the same concept of isolation/separation of fetal cells by centrifugation under “non-physiological” conditions. The prior art additional step(s) encompass(es) “ascertaining the presence of fetal NRBCs” such as subjecting cells to DNA analysis or cell sorting using antibodies and FACS within the meaning of the instant claims. Moreover, the applicant’s method as disclosed demonstrates that centrifugation step results in a possession of a cell fraction that contains fetal nucleated red blood cells (NRBCs) together with maternal nucleated lymphocytes and monocytes (specification page 10, lines 16-19; page 4, line 12). Thus, the applicant’s method as disclosed is not a single step of centrifugation that would separate or substantially separate fetal nucleated cells from all maternal mononuclear cells.

The fetal cells are identified (differentially stained and counted, see specification page 10, line 30) within the fraction of mononuclear cells comprising NRBCs and other nucleated cells. No pure preparation of fetal cells is separated, removed or obtained as disclosed. Thus, the argument drawn to the use of specific pH does not appear to be relevant for the instant invention as argued.

No claims are allowed.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

July 28, 2005

A handwritten signature in cursive script, appearing to read 'V. Afremova', with a long horizontal flourish extending to the right.

VERA AFREMOVA

PRIMARY EXAMINER